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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,824	09/08/2003	Stephen I. Rennard	UNMC/03017/0008	7805

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1657	

MAIL DATE	DELIVERY MODE
11/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,824	RENNARD ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/07/2007 has been entered.

Claims 11- 20 (4/03/2007) are pending and under examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11-14, 19 and 20 remain rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0119107 (Dang et al).

Claims are directed to a method for producing fibroblasts wherein the method comprises step of obtaining embryonic stem (ES) cells, step of culturing ES to form embryoid bodies (EB), step of isolating EB, step of casting EB in a culture medium in 3D scaffolding material that is a gel, step of growing EB in the 3D material thereby inducing differentiation to produce fibroblasts. Some claims are further drawn to the use of differentiation-inducing "cytokines"

including TGF beta or FGF. Some claims are further drawn to differentiation without addition of cytokines.

US 2003/0119107 (Dang et al) discloses a method for generation of cells or for producing cells from spheroids or from embryoid bodies wherein the method comprises step of obtaining embryonic stem (ES) cells, step of culturing ES to form embryoid bodies (EB), step of isolating EB, step of casting EB in a culture medium in 3D scaffolding material that is 3% agarose gel and step of growing EB encapsulated into the 3D material in a stirred bioreactor, for example: see abstract, par. 0120, par. 0116. Thus, the cited patent teaches method that comprises identical active steps and identical structural element as required by the claimed method.

As applied to the claims 12-14 and 19 the cited document also teaches the use of differentiation-inducing cytokines (par. 0082) including the use of TGF beta or FGF for producing mesodermal cells (table 11) that include and/or would be fibroblasts accordingly applicants' description (see instant specification page 11. par. 0034, line 7).

Thus, the cited document anticipates the presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0119107 (Dang et al) taken with Dani et al. ["Differentiation of embryonic stem cells into

adipocytes in vitro". Journal of Cell Science (1997), 110: 1279-1285] and US 6,576,464 (Gold et al.).

Claims 11-14, 19 and 20 as above. Some claims are further drawn to extraction of differentiated cells from the 3D material by digestion and centrifugation and to culturing the digested cells in monolayer culture. Some claims are further drawn to the use of media with 2% serum at step of inducing differentiation of embryonic cells and with 10% for monolayer culture.

US 2003/0119107 (Dang et al) is relied as explained above for the disclosure of a method for controlled generation of cells from embryonic stem cell-derived embryoid bodies that are encapsulated into 3D scaffold material. US 2003/0119107 teaches that cells are released from the 3D material by digestion (par. 0160). The cited document US 2003/0119107 also teaches the use of differentiation-inducing cytokines (par. 0082) including the use of TGF beta or FGF for producing mesodermal cells (table 11) that include and/or would be fibroblasts accordingly applicants' description (see instant specification page 11. par. 0034, line 7).

The cited document US 2003/0119107 discloses that in most cases differentiation inducing additives and/or factors are added to the serum-containing medium (table 10) and the disclosed protocols of culturing ES and EB encompass the use of 15% and/or 20% serum (par. 010, 0114).

US 2003/0119107 is lacking particular disclosure about the use of 2% and 10% serum containing media.

However, the cited reference by Dani et al. discloses the use of 10% serum in differentiation media in the method for culturing and differentiating embryonic cells, formation

of embryoid bodies (page 1280, col. 1, par. 3) and production fibroblast-like cells (page 1280 col. 2, par. 1, lines 17-18).

Further, US 6,576,464 teaches that differentiation of embryonic cells can be induced by withdrawal of serum or by substituting medium devoid of serum at the time of replating (col.16, lines 53-56). Thus, reduction of serum content in the medium intended for induction of differentiation would be an obvious protocol to ordinary skill practitioner at the time the claimed invention was made. One of skill in the art would have been motivated to reduce amount of serum for the expected benefits in inducing differentiation of embryonic cells as suggested by US 6,576,464. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 9/07/2007 have been fully considered but they are not persuasive.

Claim rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) has been withdrawn due to cancellation o f claims 23 and 24.

With regard to the claim rejection under 35 U.S.C. 102(e) as being anticipated by US 2003/0119107 (Dang et al) Applicants argue (response pages 4-5) that Dang et al. fail to teach every limitation of claim 11 such as casting embryoid bodies (EB) derived from embryonic stem

cells (ES) into 3D matrix and growing EB embedded in 3D matrix to induce differentiation into fibroblasts.

Upon review this argument does not appear to have any persuasive grounds with respect to the claimed invention. The cited document clearly teaches encapsulation of either or both ES and EB (see abstract) for controlled growth and the use of additives or specific environmental conditions to encourage differentiation within the broadest meaning of the claimed phrase "inducing differentiation". In the particular embodiment US 2003/0119107 (Dang et al) also clearly discloses encapsulation of EB (casting EB into 3D matrix) wherein the individual ES are cultured to induce controlled aggregation (formation of EB) and than these aggregates are encapsulated into gel (casting into 3D gel matrix), for example: see par. 0120. The cited method comprises step of obtaining embryonic stem (ES) cells, step of culturing ES to form embryoid bodies (EB), step of isolating EB, step of casting EB in a culture medium in 3D scaffolding material that is 3% agarose gel and step of growing EB encapsulated into the 3D material in a stirred bioreactor, for example: see abstract, par. 0120, par. 0116. Thus, the cited patent teaches method that comprises identical active steps and identical structural element as required for the presently claimed method and, therefore, the cited method results in the production of identical cells within the intended meaning of the claimed phrase "thereby inducing differentiation of the embryoid bodies to produce populations of fibroblasts". Furthermore, the cited document also teaches the use of differentiation-inducing cytokines (par. 0082) including the use of TGF beta or FGF for producing mesodermal cells (table 11) that include and/or would be fibroblasts accordingly applicants' description (see instant specification page 11. par. 0034, line 7). Thus,

the applicants' argument does not appear to have any persuasive grounds with respect to the claimed invention.

With regard to claim rejection under 35 USC § 103 applicants appear to argue that there is no suggestion to combine references (response page 5). However, the cited references are in the same field of endeavor (such as method of culturing and differentiation ES and EB in matrix) and they seek to solve the same problems as the instant application and claims (such as production of fibroblasts like cells), and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova, AU 1657

November 9, 2007

VERA AFREMOVA

PRIMARY EXAMINER